

β hCG

Intended use

The β hCG test is indicated for use as an aid in the early detection of pregnancy.

The test is not indicated as a surrogate marker in the diagnosis or monitoring of cancer patients.

Summary

Human chorionic gonadotropin (hCG) is a glycoprotein hormone. It is secreted during pregnancy by the trophoblastic cells of the placenta, shortly after the implantation of the fertilized ovum into the uterine wall [1,2]. Physiologically, hCG appears to maintain the corpus luteum and its synthesis of progesterone and estrogens that support the endometrium until the 4th month of pregnancy, by which time the placenta takes over the production of the hormones.



hCG appears in the blood stream 6-8 days after conception. The serum concentrations of biologically active hCG rise exponentially in the first trimester of pregnancy. It doubles every 48 hours and reaches a peak at about 10 weeks after the last menstrual period.

Concentrations decrease from the 10th to the 16th week of gestation, reaching approximately one-fifth of the peak. It remains around this concentration until the delivery [3], although there can be large individual variations in hCG concentrations. After normal delivery, the hCG concentrations decline to those observed in non-pregnant women in 1-3 weeks [4,5]. The rapid rise in hCG levels after conception makes it an excellent marker for early confirmation. hCG is also secreted by certain cancers [3]. However, this assay is not for the use in the diagnosis or monitoring of cancer patients.

Human chorionic gonadotropin is composed of two highly glycosylated dissimilar subunits, α and β , which are joined non-covalently. The subunits are rapidly disassociated and inactivated in the blood stream. Thus, both free α and β subunits together with intact hCG are found in circulation. Only intact hCG and β subunits have immunological specificity as the α subunit of hCG is similar to that of the α subunit of the pituitary glycoprotein hormones, luteinizing hormone (LH), follicle-stimulating hormone (FSH) and thyroid-stimulating hormone (TSH). The β subunit, in turn, is unique and distinguishes hCG from the other glycoprotein hormones [6].

The antibodies used in the AQT90 FLEX β hCG Test Cartridge recognize both intact hCG and free β subunits.

Product calibrator traceability

The calibration of the AQT90 FLEX β hCG assay is traceable to the Fourth International Standard for β hCG (WHO 75/589).

Samples

Blood samples are collected by venipuncture. Whole-blood or plasma samples with either EDTA or lithium heparin as anticoagulant can be used.

Performance characteristics

Analytical specificity

The analytical specificity of the AQT90 FLEX β hCG assay was determined by studying the cross-reactivity with luteinizing hormone, thyroid-stimulating hormone, follicle-stimulating hormone, placental lactogen hormone and growth hormone at concentrations of 1,000 IU/L, 175 IU/L, 1,000 IU/L, 200 μ g/L and 200 μ g/L, respectively. The cross-reactivity was shown to be less than 0.2 % in all cases.

Analytical sensitivity and measuring range

The limit of detection has been determined to be <1 IU/L.

The upper limit of the reportable range of the assay is 5,000 IU/L.

Reference values

EDTA whole blood and plasma were obtained from the following categories and analyzed using the AQT90 FLEX β hCG assay.

Patient	N	β hCG IU/L 95 % percentile
Male	255	<2
Female (all)	250	<6
Pre-menopausal	87	<2

NOTICE: These values should only be used as examples and each laboratory should establish its own reference ranges.

Imprecision

Within-day and total imprecision were determined by analyzing plasma pools over 20 days, twice a day, four replicates per run.

Within-run imprecision				Total imprecision			
Sample	Mean IU/L	SD IU/L	% CV	Sample	Mean IU/L	SD IU/L	% CV
Plasma pool 1	2.5	0.27	10.7	Plasma pool 1	2.5	0.32	12.9
Plasma pool 2	13.0	0.61	4.7	Plasma pool 2	13.0	1.00	7.7

Hook effect

No hook effect was found when β hCG concentrations up to 250,000 IU/L were measured.

Carry -over

Carry-over from a sample with a high β hCG value (100,000 IU/L) to an adjacent negative sample was determined to be <50 ppm.

Interfering substances

Hemolytic, lipemic and icteric samples do not interfere with the assay.

The following interfering substances were tested (using plasma samples with 13 IU/L of β hCG) at a concentration about five times the upper therapeutic range and found to have no notable effect on the AQT90 FLEX β hCG assay (interference <20 %):

Abciximab, acetaminophen, acetylcysteine, acetylsalicylic acid, allopurinol, ambroxol, ampicillin, ascorbic acid, atenolol, caffeine, captopril, cefoxitin, cinnarizine, cocaine, cyclosporine, diclofenac, digoxin, dopamine, erythromycin, ethanol, furosemide, low-molecular-weight heparin, sodium heparin, ibuprofen, levodopa, methyl dopa, metronidazole, nicotine (\pm), nifedipine, nitrofurantoin, nitroglycerin, nystatin, oxytetracycline, phenylbutazone, phenytoin, propranolol, quinidine, rifampicin, tetracycline, theophylline, trimethoprim, verapamil, warfarin.

Recovery

The recovery throughout the reportable range was evaluated using a negative whole-blood sample spiked with known amounts of the WHO 4th IS (75/589). The recovery ranged from -3 % to +11 %.

Method comparison

The AQT90 FLEX β hCG assay (y) was compared to the commercially available β hCG assay for the Siemens Stratus CS immunoassay system (x) using Li-heparin plasma samples in the range of 2-5,000 IU/L (with the AQT90 FLEX β hCG assay).

The linear regression line and the coefficient of determination were found to be:

$$y = 1.291 x - 7.2; R^2 = 0.984 (n = 184).$$

References

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3. Carmona F, Balasch J, Creus M et al . Early hormonal markers of pregnancy outcome after in vitro fertilization and embryo transfer. Journal of Assisted Reproduction and Genetics 2003; 20, 12: 521-26.
4. Lambers MJ, van Weering HGI, van't Grunewold MS et al. Optimizing hCG cut-off values: A single determination on day 14 or 15 is sufficient for a reliable prediction of pregnancy outcome. European Journal of Obstetrics Gynecology and Reproductive Biology 2006; 127, 1: 94-8
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